CLAIMS

What is claimed is:

1. A compound of Formula I

$$Z\text{-}L\text{-}R^1\text{-}Q\text{-}D\text{-}(V^1)_m\text{-}R^2 \qquad \text{I}$$

or a pharmaceutically acceptable salt thereof,

wherein:

Z is selected from:

HO_2C;

HO(H)N(O)C;

H(O)C-N(OH);

$CH_3(O)C$-N(OH);

$CH_3(H)N(O)C$-N(OH);

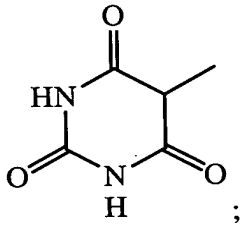
HS;

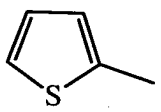
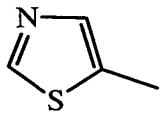
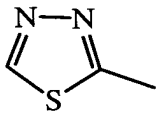
$H_2N(O)_2S$;

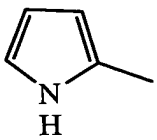
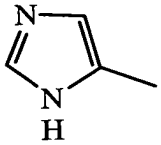
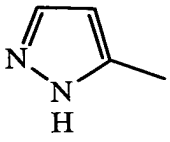
$CH_3(H)N(O)_2S$;

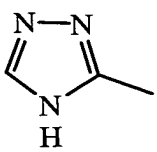
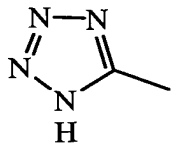
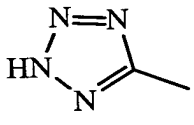
HO(O)P;

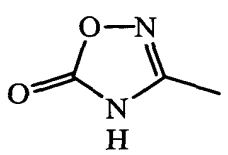
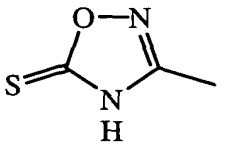
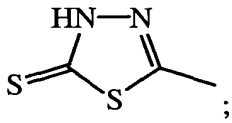
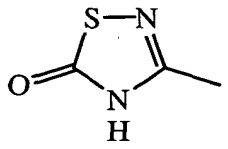
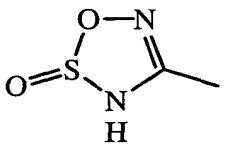
$(HO)_2(O)P$;


;


;

;

;


;

;

;


;

;

;


;

;

;

; and

;

L is selected from:

C_3-C_5 alkylenyl;

Substituted C_3-C_5 alkylenyl;

3- to 5-membered heteroalkylenyl; and

Substituted 3- to 5-membered heteroalkylenyl;

Substituted L groups contain 1 or 2 substituents on a carbon atom or nitrogen atom independently selected from:

HO;

CN; and

CF_3;

wherein each substituent on a carbon atom may further be independently F, and wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

R^1 is independently selected from:

C_5 or C_6 cycloalkylenyl-(C_1-C_8 alkylenyl);

Substituted C_5 or C_6 cycloalkylenyl-(C_1-C_8 alkylenyl);

5- or 6-membered heterocycloalkylenyl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heterocycloalkylenyl-(C_1-C_8 alkylenyl);

Phenylenyl-(C_1-C_8 alkylenyl);

Substituted phenylenyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroarylenyl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroarylenyl-(C_1-C_8 alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;

5- or 6-membered heteroaryl;

Substituted 5- or 6-membered heteroaryl;

8- to 10-membered heterobiaryl; and

Substituted 8- to 10-membered heterobiaryl;

R^2 is independently selected from:

H;

C_1-C_6 alkyl;

Phenyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

Naphthyl-(C_1-C_8 alkylenyl);

Substituted naphthyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Phenyl-O-(C_1-C_8 alkylenyl);

Substituted phenyl-O-(C_1-C_8 alkylenyl);

Phenyl-S-(C_1-C_8 alkylenyl);

Substituted phenyl-S-(C_1-C_8 alkylenyl);

Phenyl-S(O)-(C_1-C_8 alkylenyl);

Substituted phenyl-S(O)-(C_1-C_8 alkylenyl);

Phenyl-$S(O)_2$-(C_1-C_8 alkylenyl); and

Substituted phenyl-$S(O)_2$-(C_1-C_8 alkylenyl);

Each substituted R^1 group contains from 1 to 3 substituents, and each substituted R^2 group contains from 1 to 4 substituents, wherein each substituent is independently on a carbon or nitrogen atom, independently selected from:

C_1-C_6 alkyl;

CN;

CF_3;

HO;

(C_1-C_6 alkyl)-O;

(C_1-C_6 alkyl)-$S(O)_2$;

H_2N;

(C_1-C_6 alkyl)-N(H);

(C_1-C_6 alkyl)$_2$-N;

(C_1-C_6 alkyl)-C(O)O-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)O-(1- to 8-membered heteroalkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)N(H)-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)N(H)-(1- to 8-membered heteroalkylenyl)$_m$;

$H_2NS(O)_2$-(C_1-C_8 alkylenyl);

(C_1-C_6 alkyl)-N(H)$S(O)_2$-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)$_2$-$NS(O)_2$-(C_1-C_8 alkylenyl)$_m$;

3- to 6-membered heterocycloalkyl-(G)$_m$;

Substituted 3- to 6-membered heterocycloalkyl-(G)$_m$;

5- or 6-membered heteroaryl-(G)$_m$;

Substituted 5- or 6-membered heteroaryl-(G)$_m$;

(C_1-C_6 alkyl)-$S(O)_2$-N(H)-C(O)-(C_1-C_8 alkylenyl)$_m$; and

(C_1-C_6 alkyl)-C(O)-N(H)-$S(O)_2$-(C_1-C_8 alkylenyl)$_m$;

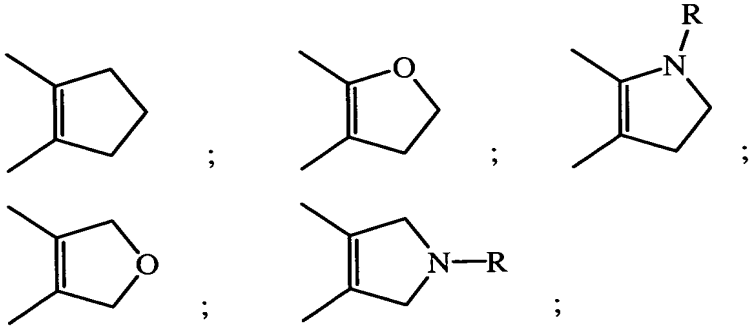
wherein each substituent on a carbon atom may further be independently selected from:

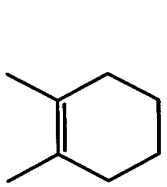
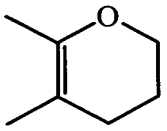
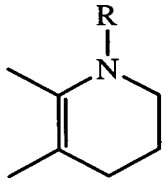
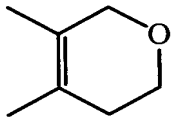
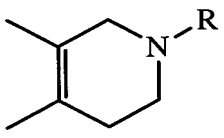
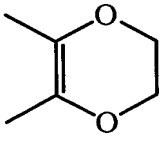
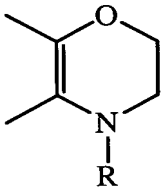
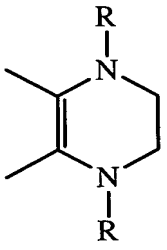
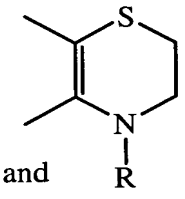
Halo; and

HO_2C;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:




;

;

;

;

;

;

;

; and

;

R is H or C_1-C_6 alkyl;

G is CH_2; O, S, S(O); or $S(O)_2$;

Each m is an integer of 0 or 1;

Q, when bonded to a nitrogen atom in group D, is selected from:

$OC(O)$;

$CH(R^6)C(O)$;

$OC(NR^6)$;

$CH(R^6)C(NR^6)$;

$N(R^6)C(O)$;

$N(R^6)C(S)$;

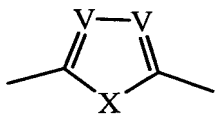
$N(R^6)C(NR^6)$;

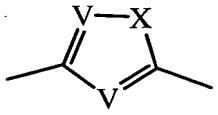
$SC(O)$;

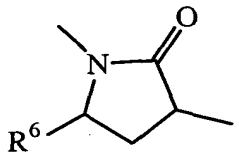
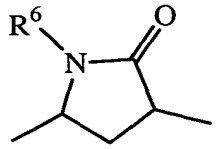
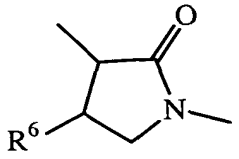
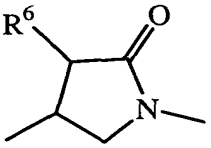
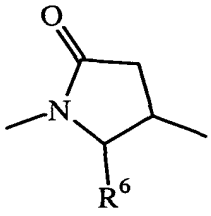
$CH(R^6)C(S)$;

$SC(NR^6)$;

$C{\equiv}CCH_2$;


;


;


;

;

;

; and

; and

Q, when bonded to a carbon atom in group D, is as defined above and may further be selected from:

OCH_2;

$N(R^6)CH_2$;

trans-(H)C=C(H);

cis-(H)C=C(H);

C≡C;

$CH_2C{\equiv}C$;

$CF_2C{\equiv}C$;

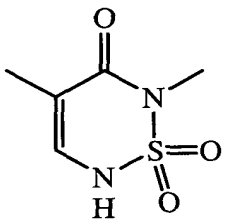
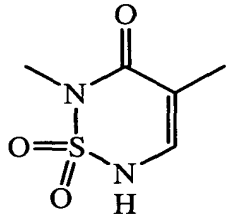
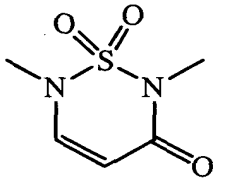
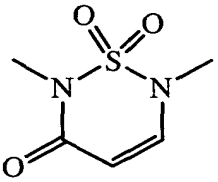
$C{\equiv}CCF_2$;

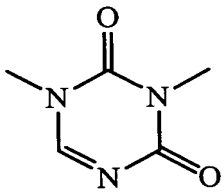
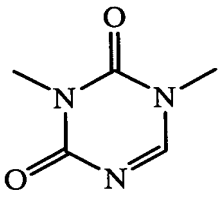
Each R^6 independently is H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl; 3- to 6-membered heterocycloalkyl; phenyl; benzyl; or 5- or 6-membered heteroaryl;

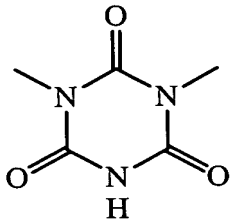
X is O, S, N(H), or N(C_1-C_6 alkyl);

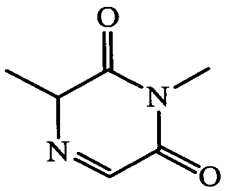
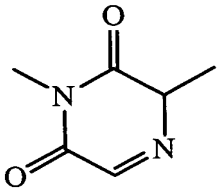
Each V is independently C(H) or N;

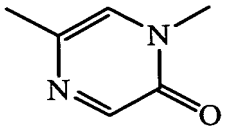
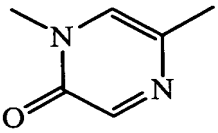
D is a cyclic diradical group selected from:

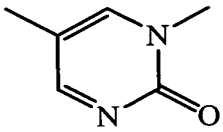
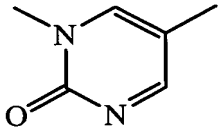

;

;

;

;

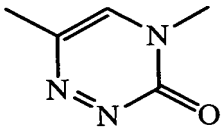
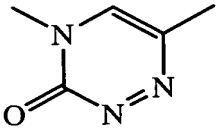

;

;

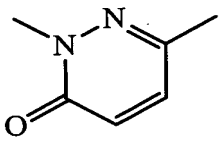
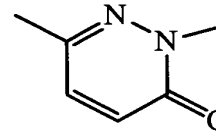

;

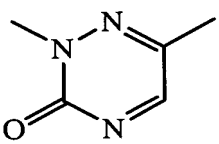
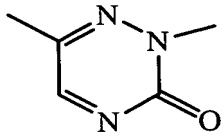

;

;

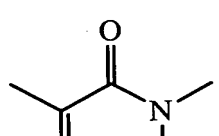
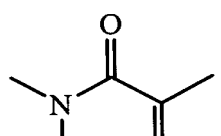

;

;

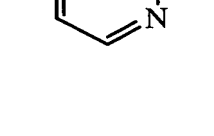
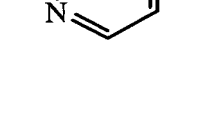

;

;

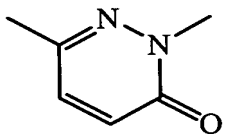
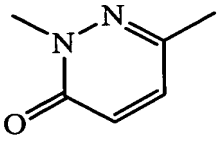

;

;

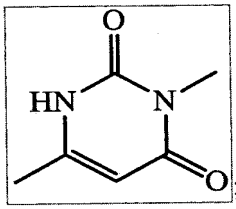

;

;

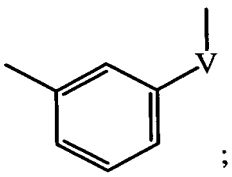
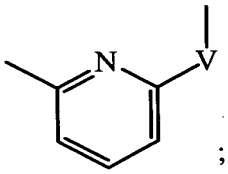
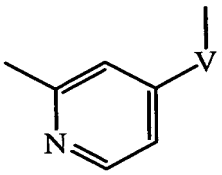

;

;

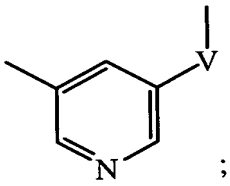
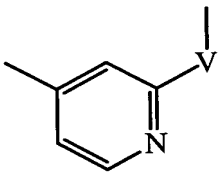
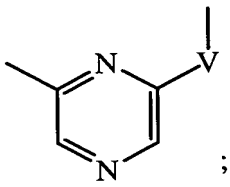

;

;

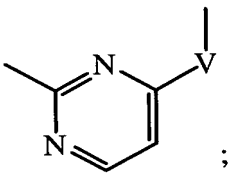
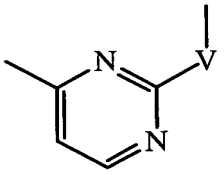
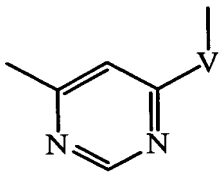

;

;

 ; and  ;

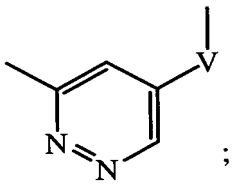
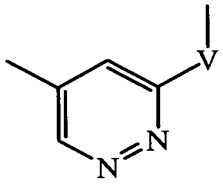
 ;

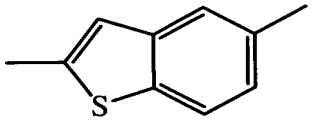
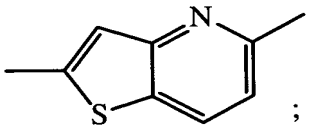
 ;  ;  ;

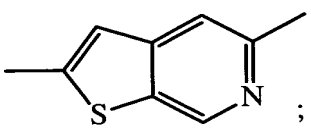
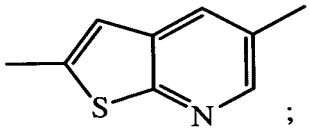
 ;  ;  ;

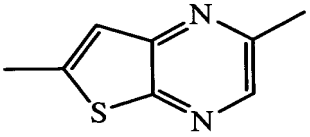
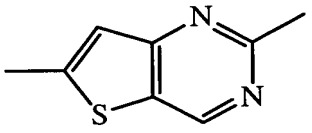
 ;  ;  ;

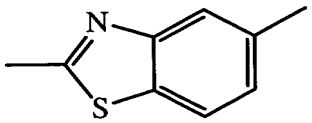
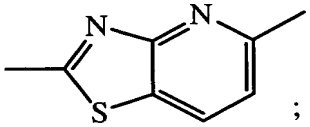
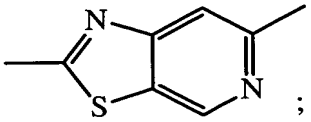
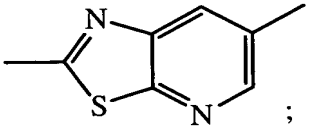
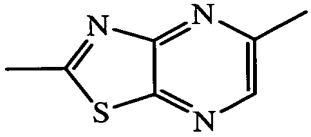
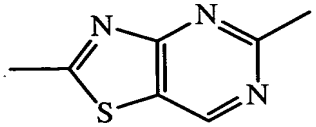
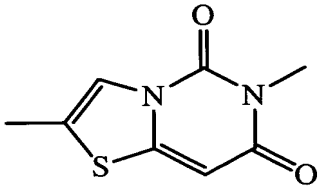
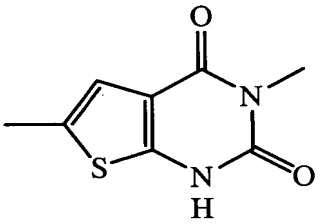
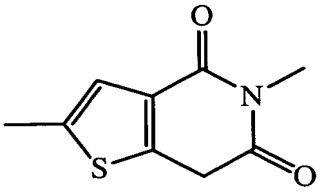
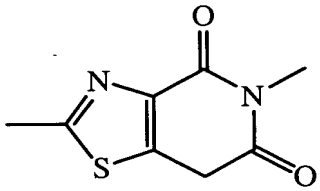
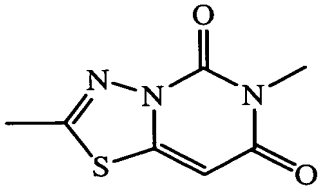
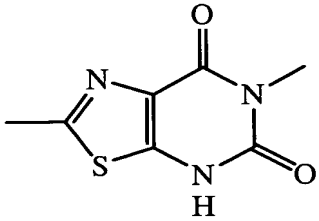
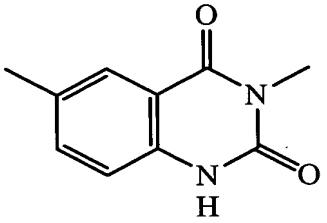
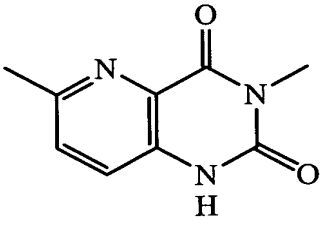
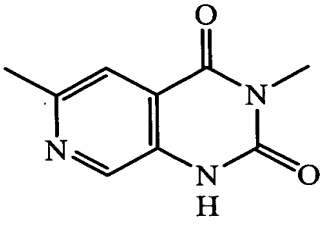
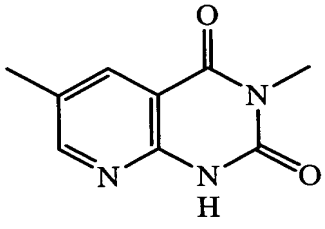
5

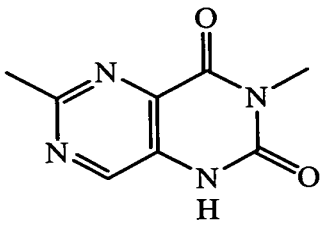
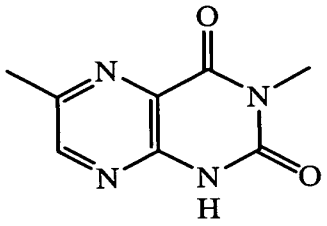
 ;  ;

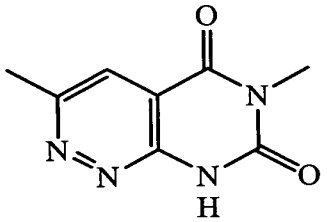
 ;  ;

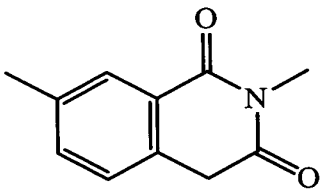
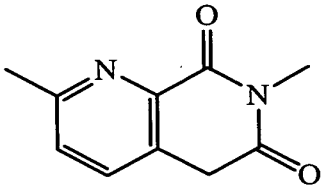
 ;  ;

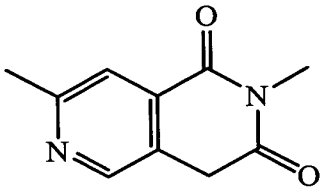
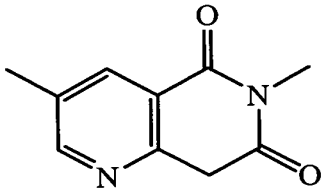
 ;  ;

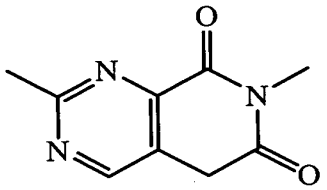
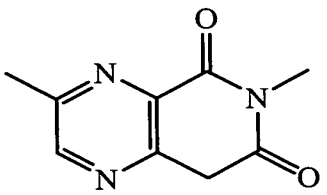

;

;

;

;

;

;

;

;

;

;

;

;

;

;

;

;

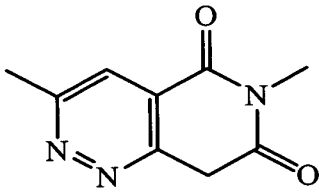

;

;

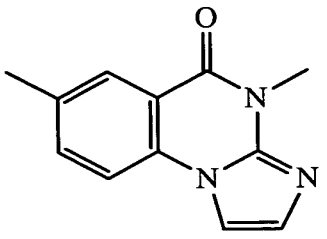
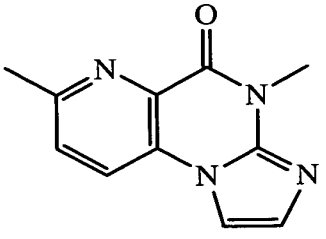

;

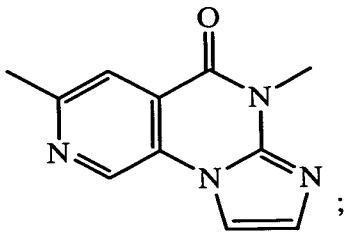
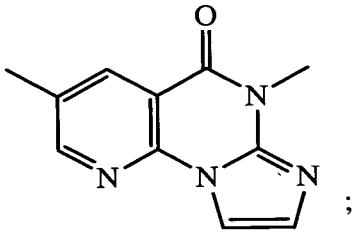
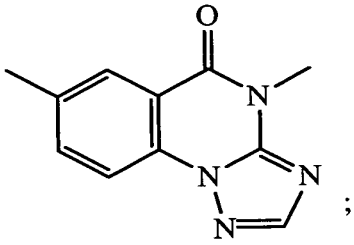
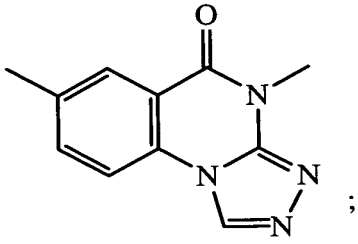
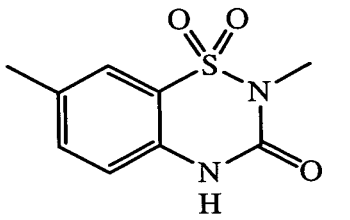
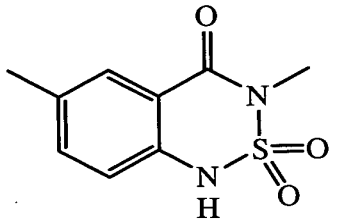
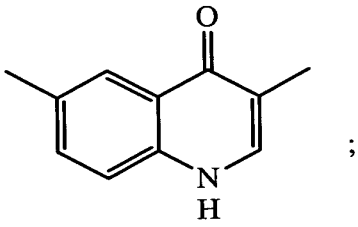
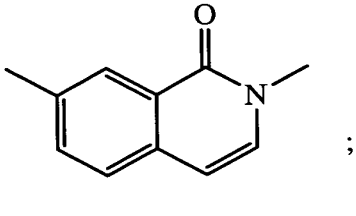
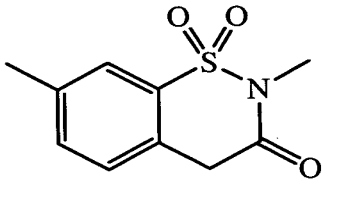
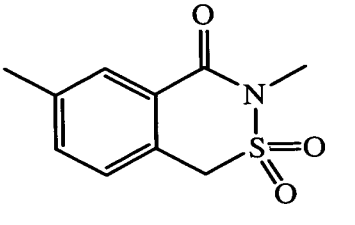
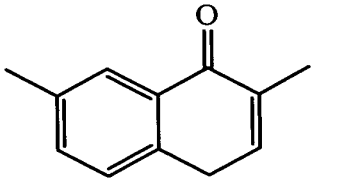
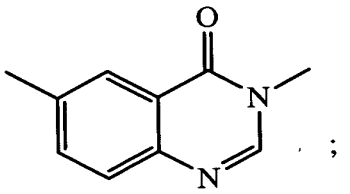
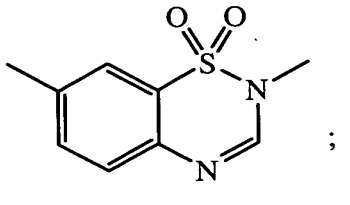

;

;

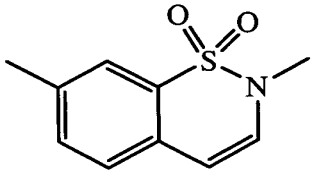

;

;

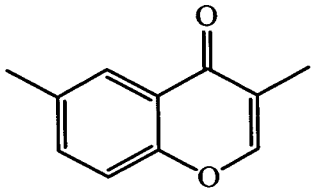

;

;

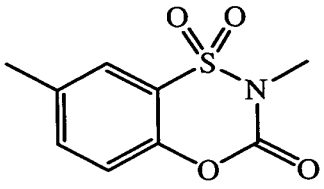

;

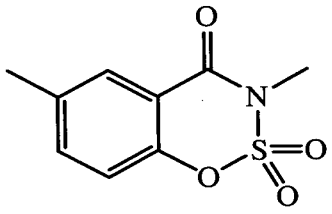

;

;

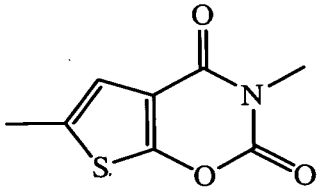

;

;

;

;

;

;

;

;

;

;
5

;

;

;

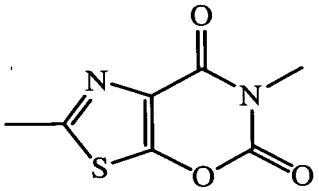

;

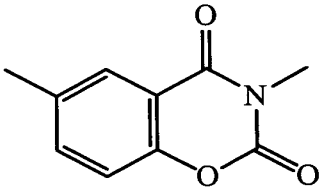

;

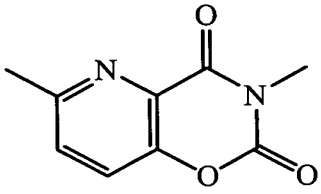

;

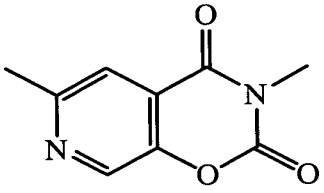

;

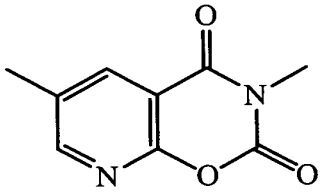

;

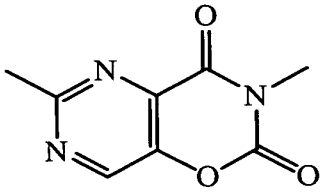

;

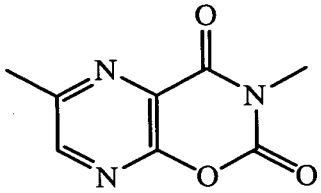

;

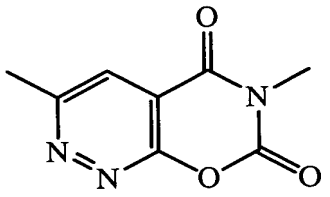

;

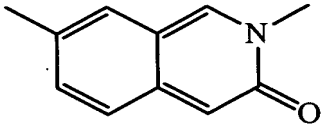

;

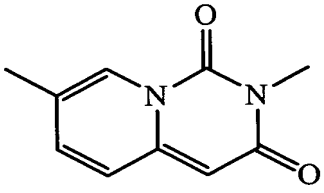

;

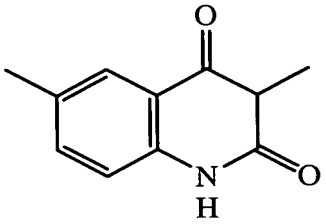

;

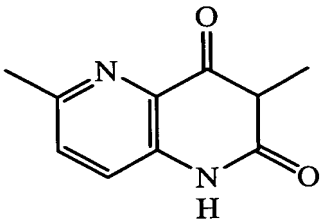

;

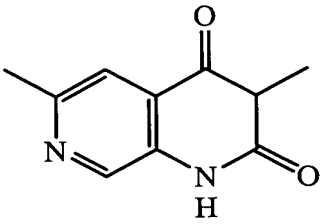

;

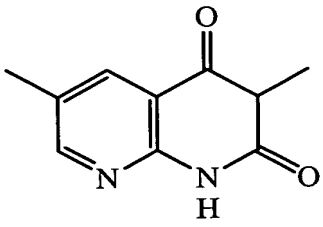

;

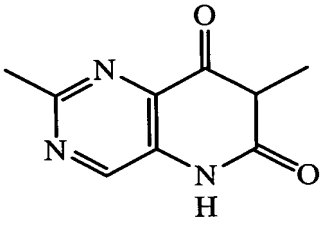

;

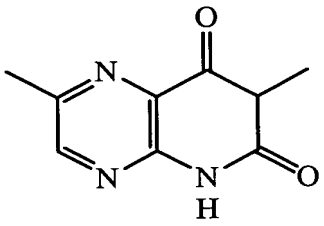

;

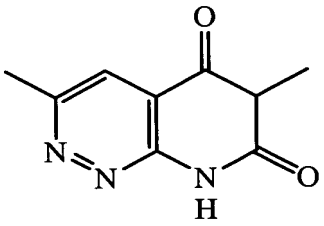

;

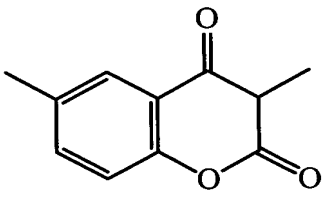
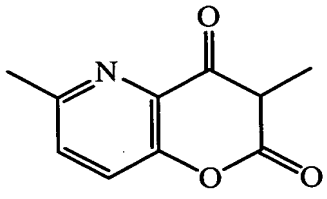
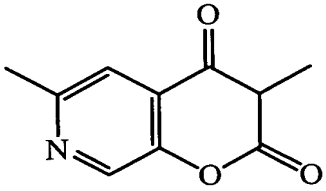
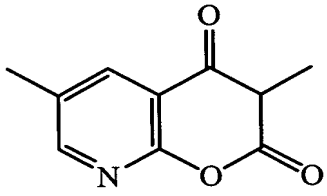
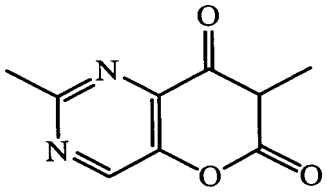
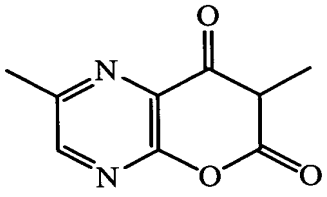
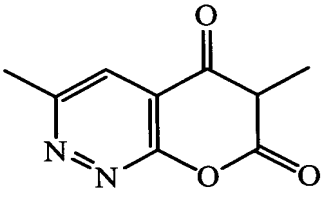
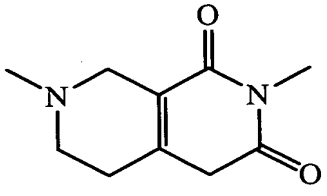
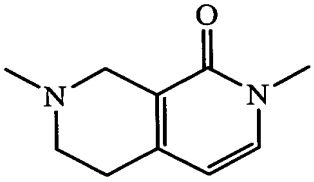
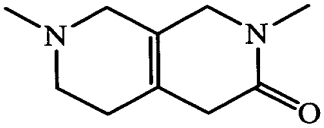
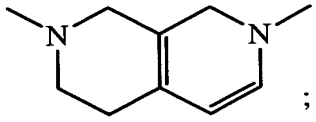
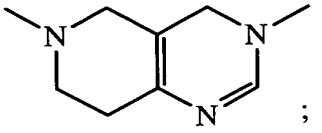
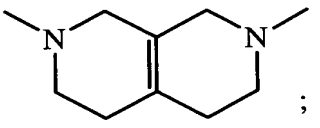

;


;


;

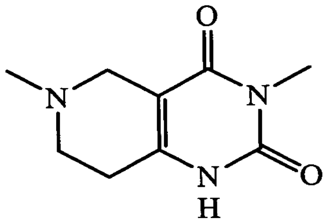

;

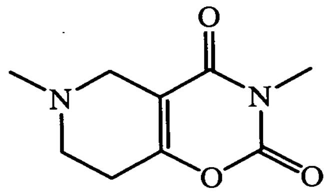

;

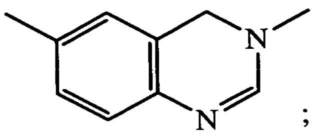

;

;

;

;

;

;

;

;

;

;

;

;

;

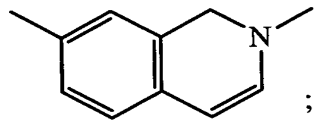
;

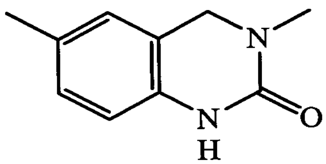
;

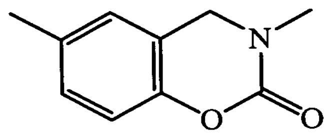
 ;

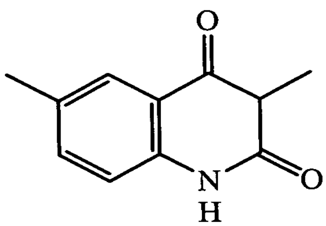
 ;

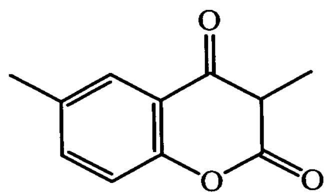
 ;

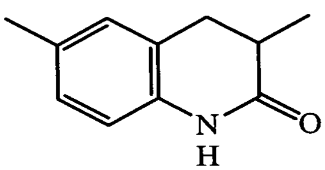
 ;

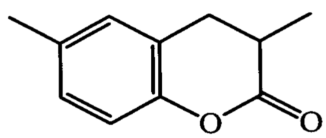
 ;

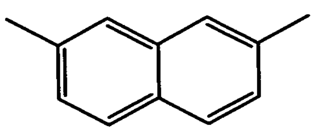
 ;

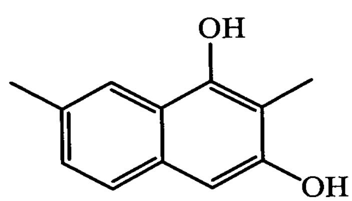
 ;

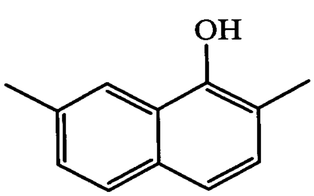
 ;

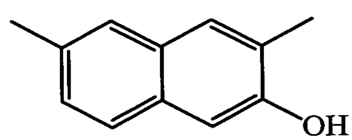
 ;

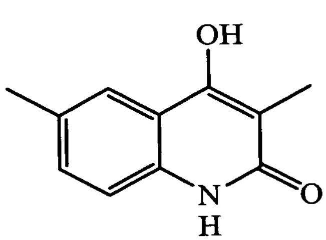
 ;

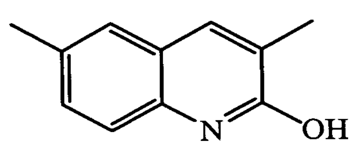
 ;

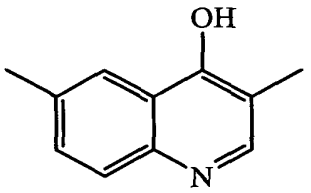
 ;

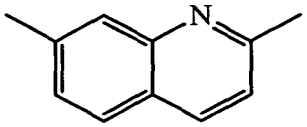
 ;

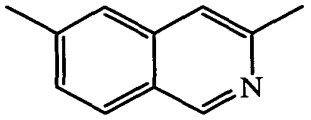
 ;

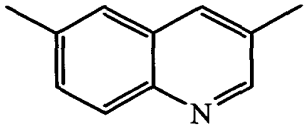
 ;

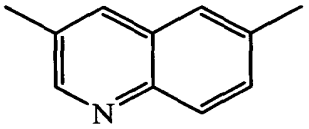
 ;

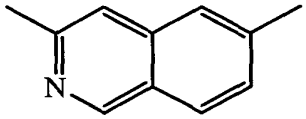


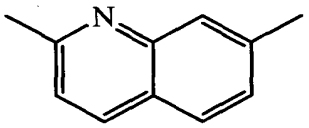
;


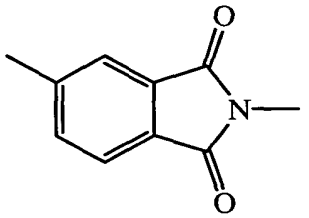
;


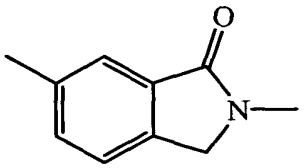
;


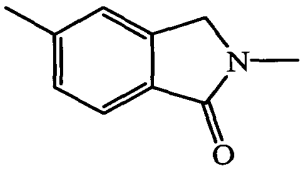
;


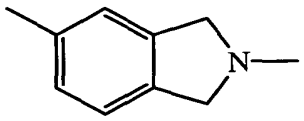
;


;


;


;


;


; and


;

wherein the group D may be unsubstituted or substituted on a carbon atom or a nitrogen atom by replacement of a hydrogen atom with a group selected from:

CH_3;

CF_3;

C(O)H;

CN;

HO;

CH_3O;

$C(F)H_2O$;

$C(H)F_2O$; and

CF_3O;

wherein a carbon atom in the group D may further be substituted with F;

V^1 is a 5-membered heteroarylenyl containing carbon atoms and from 1 to 4 heteroatoms selected from 1 O, 1 S, 1 NH, 1 N(C_1-C_6 alkyl), and 4 N, wherein the O and S atoms are not both present, and wherein the heteroarylenyl may optionally be unsubstituted or substituted with 1 substituent selected from fluoro, methyl, hydroxy, trifluoromethyl, cyano, and acetyl;

wherein each C_8-C_{10} bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 4 N(H), and 4 N(C_1-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 4 N(H), and 4 N(C_1-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each heterocycloalkylenyl is a ring diradical that contains carbon atoms and from 1 to 3 heteroatoms independently selected from 1 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 2 N(H), and 2 N(C_1-C_6 alkyl), and wherein when one O atom and one S atom are present, the one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C_1-C_6 alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein a 5-membered heteroarylenyl is a 5-membered monocyclic diradical ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, wherein the 1 O atom and 1 S atom are not both present, and 6-membered heteroarylenyl is a 6-membered monocyclic diradical ring that contains carbon atoms and 1 or 2 heteroatoms independently selected from 2 N;

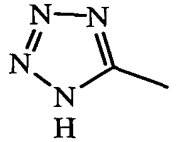
wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any (C_1-C_6 alkyl)$_2$-N group, the C_1-C_6 alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

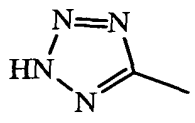
wherein each group and each substituent recited above is independently selected.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Z is HO_2C.

3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Z is selected from:

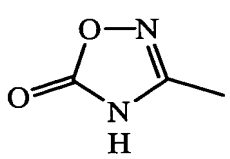
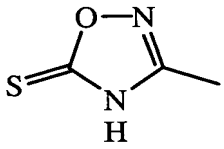


; and



.

4. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Z is selected from:

 ; and  .

5. The compound according to any one of Claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein Q is $N(R^6)C(O)$.

6. The compound according to any one of Claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein Q is selected from:

$C\equiv C$;

$CH_2C\equiv C$;

$C\equiv CCH_2$;

$CF_2C\equiv C$; and

$C\equiv CCF_2$.

7. The compound according to Claim 1, selected from:

4-(3-{3-[3-(3,4-Difluoro-benzyl)-4-oxo-3,4-dihydro-quinazolin-6-yl]-prop-2-ynyl}-phenyl)-butyric acid; and

5-(3,4-Difluoro-benzyl)-7-methyl-4,6-dioxo-3a,4,5,6-tetrahydro-thieno[3,2-c]pyridine-2-carboxylic acid [2-(3-mercapto-propoxy)-pyridin-4-ylmethyl]-amide;

or a pharmaceutically acceptable salt thereof.

8. A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

9. The pharmaceutical composition according to Claim 8, comprising a compound according to Claim 7, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

10. A method for treating osteoarthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

11. The method according to Claim 10, wherein the compound administered is a compound according to Claim 7, or a pharmaceutically acceptable salt thereof.